leukemia that contained insertions in both *LMO2* and *gamma c*, the gene corrected by the X-SCID therapy (*Science*, 16 January 2004, p. 333). The two genes seem to "cooperate" in causing cancer, Davé said, suggesting that gene therapy for diseases not involving *gamma c*—which itself may be oncogenic when expressed by a retrovirus—may be safer.

Indeed, panelists noted, no leukemia cases have yet been seen in trials of ADA-SCID, which does not involve the *gamma c* gene. Nor have leukemias appeared in an X-SCID trial in the United Kingdom that has treated 7 patients. However, the French leukemias appeared roughly 33 months after treatment, and the U.K. patients have not reached that point.

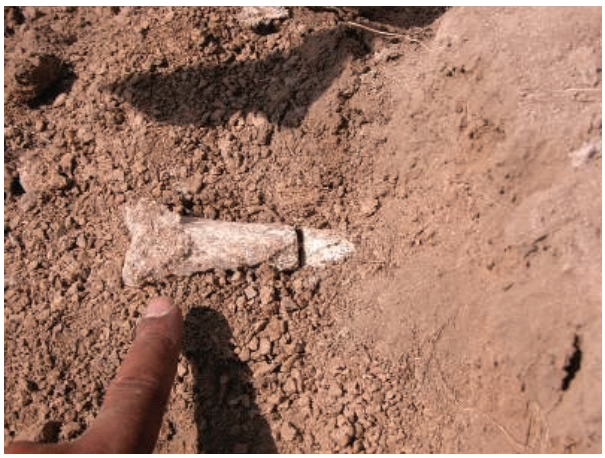
The panel concluded that if two X-SCID trials now on hold in the United States resume, they should enroll only children who have failed bone marrow transplants. "That's going to be a very small number," said panelist Daniel Salomon of the Scripps Research Institute in La Jolla, California. But the panel suggested FDA could lift its hold on a U.S. trial for ADA-SCID. Researchers will be watching closely to see whether any leukemia cases turn up in the British trial. If not, "that would certainly change things" because it would suggest conditions specific to the French trial are leading to the leukemias, concluded Rao.

–JOCELYN KAISER

PALEOANTHROPOLOGY

Skeleton of Upright Human Ancestor Discovered in Ethiopia

Scientists working in the remote badlands of Ethiopia have found the oldest known skeleton of an upright walking hominid, roughly dated to nearly 4 million years ago. The remarkably preserved partial skeleton includes many bones of the pelvis, leg, back, and arms, as a team led by paleoanthropologists Yohannes Haile-Selassie and Bruce Latimer of the Cleveland Museum of Natural History in Ohio announced last week at a press conference in Addis Ababa, Ethiopia.



Early walker. The owner of this shinbone walked upright in Ethiopia 4 million years ago.

CREDIT: ANTHONY MITCHELL/AP PHOTO

The shape of the top of the lower leg bone and pelvis have already convinced the discoverers that this hominid walked on two legs, which is the traditional hallmark of being a member of the human family rather than an ancestor of apes. "It's a once-in-a-lifetime discovery," says Haile-Selassie.

The skeleton so far also includes precisely the anatomical parts below the neck that can allow scientists to distinguish whether it walked like a modern human or in a more primitive manner. "It's a monumentally important skeleton, a real key to understanding hominid origins," says paleoanthropologist Carol Ward of the University of Missouri, Columbia, who cautions that she has not seen the as-yet-unpublished skeleton. "The bits from the skeleton are exactly the pieces we need to see if we came from something like a chimp or something more primitive."

The skeleton was found on 10 February near the village of Mille in the central Afar Depression, where a sharp-eyed fossil hunter named Alemayehu Asfaw spotted an elbow bone. Soon team members found the other part of the arm bone, the pelvis, leg bones, ribs, vertebrae, clavicle, and scapula. Extinct pigs found with the skeleton suggest that it lived 3.8 million to 4 million years ago, a critical time when humans were evolving the ability to walk. The team is now dating samples of volcanic rock taken from layers above and below the fossil and studying fragmentary fossils, including leg and toe bones, from 11 other individuals.

The identity of the new skeleton is still unclear, in part because the specimens are still embedded in matrix and also because most of the known fossils of this age are so fragmentary. There are only four other partial skeletons of human ancestors older than 1 million years. Contenders for the new skeleton's identity include the slightly younger *Australopithecus afarensis*, whose most famous member is Lucy, a partial skeleton that lived 3.2 million years ▶

ScienceScope

Brazil OKs Stem Cell Work

The way is clear for Brazilian scientists to work with human embryonic stem (ES) cells. On 3 March, the Brazilian legislature passed a wide-ranging biosecurity bill that legalizes work with the cells, sending it to President Luiz Inácio Lula da Silva for his signature. It allows scientists who receive permission from a national ethics board to work with existing ES cell lines and to derive new ones from frozen embryos left over after fertility treatments. It also outlaws nuclear transfer experiments using human cells.

Geneticist Mayana Zatz of São Paulo University says she hopes to begin work soon on muscle and nerve studies using ES cells. The bill also allows for the sale of genetically modified seeds.

–GRETCHEN VOGEL

New Trade Rules on Sturgeon

The world's most valuable fish—the beluga sturgeon, a target of human predators who sell its eggs for $100 an ounce—may get help from the U.S. Fish and Wildlife Service (FWS). Officials ruled last week that nations wishing to continue selling beluga caviar to the United States (which consumes 80% of legal exports) must file plans with FWS in 6 months showing how they will stem the species' decline. Those that don't comply will face a trade ban on the fish. Most directly affected are Kazakhstan, Iran, and Russia. Environmentalists decry the new rule, urging an immediate U.S. import ban.

–CHRISTOPHER PALA

Insider Nominated to EPA

A nominee to lead the Environmental Protection Agency (EPA) has succeeded in gaining the unlikely support of both environmentalists and industry groups.

Last week President George W. Bush chose Stephen Johnson, 53, to replace Michael Leavitt as head of EPA. Johnson, who holds a master's degree in pathology, would be the first administrator with scientific training.

Those pleased by the decision include the Environmental Working Group and a pesticide trade group called CropLife America, both based in Washington, D.C.

"He's coming into the job with a stronger grasp of the science than any past administrator," says Lynn Goldman of Johns Hopkins Bloomberg School of Public Health in Baltimore, Maryland. The main question, she adds, is whether he will have any clout in the White House.

–ERIK STOKSTAD

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ago at Hadar, 60 kilometers south of Mille. An older Kenyan species thought to be bipedal, 4.1-million-year-old *A. anamensis*, is also a possibility. Haile-Selassie says the new skeleton is slightly younger and distinct from the mysterious 4.4-million-year-old *Ardipithecus ramidus*, known from teeth and a crushed, still unpublished, skeleton that he also found; he adds that the new skeleton may connect the dots between *Ardipithecus* and later australopithecines, revealing how the human mode of walking evolved. Three even earlier species have been proposed as bipedal hominids but are known only from fragmentary fossils or a skull.

The discovery of the new skeleton comes at a good time for Haile-Selassie, one of the first black Africans to launch his own fossil-hunting expedition (*Science*, 29 August 2003, p. 1178). The U.S. National Science Foundation rejected his grant application last year to look for hominids in the localities around Mille. Instead, he and Latimer got foundation funding for a small team of mainly Ethiopian fossil hunters. With a find like this, Haile-Selassie hopes getting future grants will not be a problem. "We want to go out and see if we can find the head and mandible," he says. **–ANN GIBBONS**

ALZHEIMER'S DISEASE

Play and Exercise Protect Mouse Brain From Amyloid Buildup

As the population ages, finding ways to stave off the debilitating brain degeneration of Alzheimer's disease becomes ever more critical. New results with a mouse model of the condition now provide further support for the idea that "use it or lose it" applies as much to the mind as to the body.

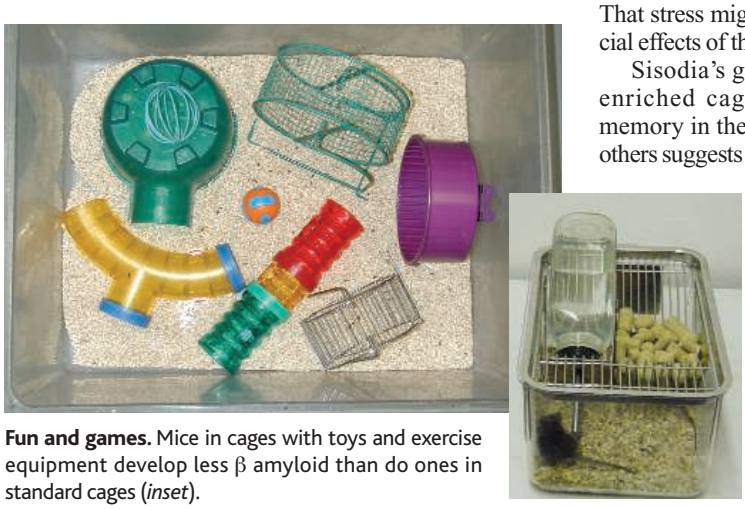
A leading explanation for Alzheimer's disease blames abnormal buildup of a small protein called β amyloid, which accumulates in pathological structures called plaques in patients' brains. Now, working with mice genetically engineered to produce similar β-amyloid plaques, a research team led by Sam Sisodia of the University of Chicago, Illinois, has found that the β-amyloid buildup can be greatly reduced by a lifestyle change: housing the animals in an enriched environment—one amply stocked with toys and exercise equipment—instead of in standard lab cages equipped with nothing more than food, water, and bedding material.

The experiments, reported in today's issue of *Cell*, also provide clues to how an enriched environment might protect against β-amyloid accumulation. Zaven Khachaturian, editor of the journal *Alzheimer's and Dementia*, calls the work "very provocative. … It opens new ways of getting at the underlying mechanism" of plaque formation.

Several epidemiological studies have suggested that environmental enrichment, including education and intellectually challenging leisure activities such as reading and playing bridge, diminishes the risk of Alzheimer's disease. Others have pointed to a possible protective role of exercise. But lower activity levels could be an early symptom of the disease rather than a risk factor.

With mice, though, it's possible to study environmental influences on the earliest stages of plaque formation. Sisodia and his colleagues Orly Lazarow and John Robinson started their experiments when the mice were just 1 month old, many weeks before they normally show symptoms of Alzheimer's disease; the genetically modified animals they used ordinarily develop β-amyloid plaques by about 4.5 months of age. The researchers put seven animals in standard cages and another nine in the enriched environment, where the activities of the mice were closely monitored.

After 5 months, the researchers killed both sets of mice and examined their brains. Animals kept in the enriched environment showed "a marked reduction in amyloid burden," Sisodia says. The decrease appeared to be related to exercise. "The animals that were most active as determined by their time on the running wheels had the least [β-amyloid] burden," Sisodia adds. He notes, however, that other aspects of the enrichment, such as increased visual stimuli and social interactions, could still account for the reductions.



Fun and games. Mice in cages with toys and exercise equipment develop less β amyloid than do ones in standard cages (*inset*).

CREDITS: ORLY LAZAROW, JOHN ROBINSON, AND SANGRAM S. SISODIA

The researchers also identified changes in the brain that might explain a lessening of β-amyloid deposition. They saw increased activity of a β-amyloid–degrading enzyme called neprilysin in the brains of the enriched mice, as well as changes in gene expression that could promote neuronal survival and enhance learning and memory.

In late 2003, Joanna Jankowsky of the California Institute of Technology in Pasadena, David Borchelt of the Johns Hopkins University School of Medicine in Baltimore, Maryland, and their colleagues reported that enriched environments actually increase plaque formation. The reason for the discrepancy is unclear, although the design of the 2003 experiment was different. For one, that study involved only female mice, whereas the Sisodia team used males. The Jankowsky-Borchelt group also had many more animals in their enriched cages and added young mice as they removed older ones. "To me that spells stress," says David Arendash of the University of South Florida in Tampa, who also studies the effects of enrichment on Alzheimer's mice. That stress might have overcome any beneficial effects of the enhanced environments.

Sisodia's group didn't test whether the enriched cages improved learning and memory in their animals, although work by others suggests that it may. This was the case in the experiments performed by Arendash. The improvement occurred even though the Tampa team did not see reductions in β-amyloid deposition in their mice. But those animals were very old—16 months at the start of enrichment—and they already had extensive β-amyloid deposition.

How much these mouse studies of enriched environments relate to Alzheimer's disease in people remains to be seen. Adding another clue, Constantine Lyketsos and his colleagues at the Johns Hopkins Medical Institutions in Baltimore will report in the April issue of the *American Journal of Epidemiology* that engaging in a variety of different physical activities can reduce the risk of developing Alzheimer's disease by as much as 50%, although only in people who did not carry a particular gene variant called *APOE4* that increases Alzheimer's risk.

Lyketsos says that his team's results and Sisodia's provide an "interesting convergence" about the possible effects of physical exercise on Alzheimer's risk. So while you're out running to save your heart, you might also be saving your brain. **–JEAN MARX**

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